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09/030,482	02/25/1998	TERRY P. SNUTCH	NMED.P-001	7416

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EXAMINER	
BASI, NIRMAL SINGH	
ART UNIT	**PAPER NUMBER**
1646	27

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/030,482	Snutch et al
Examiner	**Art Unit**
Nirmal S. Basi	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Sep 5, 2001 .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 28-34 is/are pending in the application.

4a) Of the above, claim(s) 34 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 28-33 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. In response to applicant's telephonic request to further clarify the issues addressed in the Office Action dated 10/23/01, paper number 26, a supplemental action is set forth below:

The period for reply of 3 MONTHS set in said Office action is restarted to begin with the mailing date of this letter.

2. The request filed on 9/5/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53 (d) based on parent application No. 09/030,482 is accepted and a CPA has been established. An action on the CPA follows

3. Amendment filed 4/9/01, Amendment filed 6/11/01 and Declaration filed 6/11/01 have been entered.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action (51/17/01, paper number 14).

Response to Amendment with new claims

5. Applicant has canceled claims 16-27, previously present in the Application and amended claims 28-33 and added new claim 34. Newly added claims 34, will not be examined. Since applicant has received an action on the merits for the originally presented invention (Group I), this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 34, drawn to a method to obtain an isolated DNA molecule encoding a

functional α1 subunit of a T-type calcium channel, using PCR is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejection, 35 U.S.C. 112, second paragraph

6. Claims 28-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection of Amended claim 28, is maintained in view of the old claim 28, that was rejected in the Office Action mailed 1/17/01, paper number 14, and in view of the rejection that was restated to better address the Amended claim 28 in the Office Action mailed 10/23/01, paper number 26. The rejection of Amended claim 28, 32 and 33, is a new rejection and is made to better address the rejection of Amended claims 28, 32 and 33 (amended claims recite "functional" language) and further clarifies the rejection stated in the Office Action mailed 10/23/01, paper number 26. Claims 29, 30, 31 are indefinite for depending on a base claim or intermediate claim and fail to resolve the issues raised in the base or intermediate claim on which they depend.

Summary of applicant's arguments:

Applicant argues that medium stringency is art standard and represents a narrow range of conditions that one of ordinary skill in the art would understand what is meant by medium stringency conditions.

Applicant argues that the α1 subunit has been defined.

Applicants arguments have been fully considered and found persuasive in part.

Response to Applicants specific arguments

The rejection of Amended claim 28, is maintained in view of the old claim 28, that was rejected in the Office Action mailed 1/17/01, paper number 14, because "Medium hybridization stringency" conditions are not disclosed. Applicant states, "Applicants have already, in the previous response, submitted a declaration indicating that one of ordinary skill in the art would understand what is meant by medium stringency conditions. These conditions represent a narrow range of conditions which is contrasted with high stringency and low stringency. These are conventional terms in the art. It is not clear from the rejection whether the office believes the term "medium stringency" is not supported in the specification; however, this terminology is specifically supported in the specification at pages 14-15, bridging sentence". Applicants arguments have been fully considered but not found persuasive. The specification at pages 14-15, bridging sentence states, "The screening of cDNA libraries follows standard methods and includes such protocols as infecting bacteria with recombinant lambda phage, immobilizing lambda DNA to nitrocellulose filters and screening under medium hybridization stringency conditions with radiolabelled probe". The metes and bounds of the group of polynucleotides that would meet the limitations of the claim depend upon the precise conditions under which hybridizations were performed, including wash conditions. Hybridization conditions of temperature, salt and time all determine the polynucleotides that remain bound to the DNA of Claim 28 (a). Although medium stringency conditions represent a narrow range of conditions which can be contrasted with high stringency and low stringency, without a specific disclosure of the high stringency and low stringency conditions the metes and bounds of

medium stringency conditions cannot be determined. The disclosure by Dr. Terry P. Snutch does not overcome the deficiency in the specification which does not specifically disclose medium hybridization stringency conditions, used in instant claims. To determine the metes and bounds of medium stringency hybridization what is required are the specific conditions that form the lower limit of medium stringency hybridization conditions and those conditions that form the upper limit of medium stringency hybridization, none of which are disclosed. Therefore the term medium stringency hybridization represents the range of conditions X-Y, where X is the lower limit and Y is the upper limit. The question is what conditions of temperature , salt concentration and time represent X and those that represent Y, so as to allow the metes and bounds of the claim to be determined. To overcome examiners rejection, it is suggested, Applicant remove "medium hybridization stringency" and incorporate language that limits the claim by reciting hybridizing coupled with descriptive structural and functional limitations.

Amended claims 28, 32 and 33 are indefinite (new rejection which further clarifies the rejection of Amended claims 28, 32 and 33 and was presented in paper number 26, 10/23/01) because it is not clear what is the "functional T-type" calcium channel $\alpha 1$ subunit, so as to allow the metes and bounds of the claims to be determined. The function of the $\alpha 1$ subunit encoded by the polynucleotide of SEQ ID NO:18 of has not been disclosed and therefore the metes and bounds of the claim cannot be determined. The specification and Applicants Response filed 6/11/01 disclose the "amino acid sequence encoded by SEQ ID NO:18 is not complete", and lacks a small portion of the amino acid sequence which is required to obtain functionality (See paper number 23, page 4,

second paragraph). Since the protein encoded by the polynucleotide sequence of SEQ ID NO:18 is not functional it is not clear what else in addition to the sequence disclosed is required to form the "functional" calcium channel α1 subunit.

The rejection of the use of the name α_1 subunit in claims 28, 32 and 33 is withdrawn in view of Applicants arguments and Amendments filed 6/11/01.

Claims 29, 30, 31 are indefinite for depending on a base claim or intermediate claim and fail to resolve the issues raised above.

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph

8. The rejection of Amended claims 28-33 is maintained under 35 USC § 101 and 35 USC § 112, 1st paragraph, in view of the old claims 28-33, that were rejected in the Office Action mailed 1/17/01, paper number 14, and in view of the rejection that was restated to better address the Amended claims 28-33 in the Office Action mailed 10/23/01, paper number 26.

A summary of Applicants arguments is listed below:

Applicant and the Declaration of Dr. Snutch (6/11/01) have argued that a specific or substantial utility has been provided in the specification and the Examiner reconsider and withdraw the rejection. Applicants and the Declaration of Dr. Snutch have been fully considered but not found persuasive .

Applicant argues that the instant "alpha-subunit" is useful to screen libraries for compounds which agonize or antagonize the T-type calcium channel and that antagonists may be used to treat conditions associated with abnormal T-type calcium channel activity

Applicant lists several conditions known in the art to be associated with T-type calcium channels including cardiac hypertrophy, hypertension, convulsions, epilepsy, and impaired fertility.

Applicant argues that an antagonist of one T-type channel is an antagonist for all T-type channels and therefore the screening method is specific and is applicable to them all and would be useful in treating any condition associated with any T-type channel.

Applicant argues that the mere fact that this utility is a research tool does not disqualify it from being a substantial utility and does not compare to the situation in *Brenner v. Manson*.

Applicant argues that there is no per se rule that partial DNA sequences lack utility and that methods of identifying the full length sequence have utility. Applicant argues that SEQ ID NO: 18 encodes most of the alpha subunit required for function and that enough information is provided to complete the sequence.

Applicant argues that no *prima facie* case of lack of credible utility has been set forth by the office.

A summary of the claimed invention is given below:

The specification discloses the $\alpha 1$ subunit of a human calcium channel protein, encoded by claimed DNA molecule, is incomplete (i.e. does not contain the complete sequence) and lacking functionality. Applicants Response filed 6/11/01 verifies the "amino acid sequence encoded by SEQ ID NO:18 is not complete", and lacks a portion of the amino acid sequence which is required to obtain functionality (See paper number 23, page 4, second paragraph). Therefore, by Applicants own

admission, the claimed polynucleotide encoding the polypeptide of SEQ ID NO:18, is incomplete. Applicant further admits, page 6, the polypeptide is missing "approximately 400 amino acids". Therefore, even though the missing sequence may turn out to be homologous or similar to the C-terminus of other channel proteins, further experimentation is required to complete the missing sequence and determine functionality. Although α1 subunits of calcium channel protein alone can form functional calcium channels, as stated on page 5, lines 15-18, the fact that their electrophysiological and pharmacological properties can be differently modulated by coexpression with any of the four β subunits argues that effects of calcium channel modulation will vary in the native state depending on the availability of four β subunits. The possibility exists that other sub-units, in addition to the ones known may have to be discovered which are required to confer functionality on the claimed α1 subunit. The specification nor prior art disclose any ligands, agonists or antagonists that bind or affect the functionality of the claimed DNA encoding the α1 subunit of a human calcium channel protein. Further the specification, on page 9, discloses, "since defects in the novel calcium channel subunits may be associated with a human genetic disease including, but not limited to; epilepsy, migraine, ataxia, hypertension, arrhythmia, angina, depression, small lung carcinoma, Lambert-Eaton syndrome, characterization of such associations and ultimately diagnosis of associated diseases can be carried out with probes which bind to the wild-type or defective forms of the novel calcium channels". There is no disclosure of any specific disease states associated with dysfunction of claimed DNA encoding the α1 subunit of a human calcium channel protein or defective forms of said protein.

Response to Applicants specific arguments

Applicants argument that the instant "alpha-subunit" is useful to screen libraries for compounds which agonize or antagonize the T-type calcium channel and that antagonists may be used to treat conditions associated with abnormal T-type calcium channel activity have been fully considered but not found persuasive. Since the functionality of the T-type calcium channel has not been disclosed there is no activity that can be screened. The protein encoded by claimed DNA is incomplete and does not form a functional calcium channel and therefore cannot be used in a functional assay where calcium transport is measured. There are no known agonists for the claimed calcium channel therefore the effect of antagonists cannot be determined. Applicant has not disclosed any antagonists or agonists that bind to the protein encoded by claimed DNA that may be used to treat conditions associated with T-type calcium channels or any specific disease states or dysfunctions treatable with said agonists and antagonists. Without knowledge of the functionality of the claimed invention, it is not clear to the Examiner, how one can make the assumption that an antagonist will treat a specific condition. Dysfunction of a calcium channel may be caused by increased or decreased channel activity, therefore a conclusion that an antagonist will treat a disease state is incorrect, the agonist may be required.

Applicant lists several abnormal conditions known in the art to be associated with T-type calcium channels including cardiac hypertrophy, hypertension, convulsions, epilepsy, and impaired fertility but does not disclose the specific condition associated with dysfunction of claimed calcium channel. Applicant has generally argued the general nature of calcium channels and in essence

verifies the Examiners position to the complex nature of calcium signaling, the diversity of the effects of calcium in signaling mechanisms and the effects of the various calcium channels in signaling mechanisms is dependent on the specific calcium channel. Since all calcium channels are not involved with the same disease state and electrophysiological and pharmacological properties can be differently modulated by the β subunits and the cell environment, the effects of calcium channel modulation will vary with cell type and specific calcium channel. Therefore an association between the claimed T-type calcium channel and an associated dysfunction cannot be made based on the specification and prior art.

Applicant argument that an antagonist of one T-type channel is an antagonist for all T-type channels and therefore the screening method is specific and is applicable to them all and would be useful in treating any condition associated with any T-type channel has been fully considered but not found persuasive. Since the functionality of the claimed calcium channel is not known, what does the antagonist antagonize? Applicant has disclosed many diverse disease states associated with T-type calcium channel dysfunction, antagonists of many calcium channels activity are known, there is no disclosure in the prior art that a single antagonist can treat all the diverse number of diseases Applicant states are associated with calcium channel dysfunction, i.e. epilepsy, migraine, ataxia, hypertension, arrhythmia, angina, depression, small lung carcinoma. Lambert-Eaton syndrome, cardiac hypertrophy, convulsions, epilepsy, and impaired fertility, absent evidence to the contrary.

Applicant arguments that the mere fact that this utility is a research tool (screening tool) does not disqualify it from being a substantial utility and does not compare to the situation in *Brenner v.*

Manson have been fully considered but not found persuasive. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a DNA encoding a partial protein of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the claimed DNA was, as of the filing date, useful for diagnosis, prevention and treatment of an disease, or for screening compounds. Until some actual and specific significance can be attributed to the protein identified in the specification as SEQ ID NO:19, or the gene encoding it, one would have to perform further research on the claimed invention in order to determine how to use the claimed invention, which contrasts with a use as a tool. Thus, there was no immediately

apparent or "real world" utility as of the filing date. Further Applicant argues all T-type calcium ion channels have the same connection to disease states and therefore the utility is specific. The connection to the disease state has not been shown. The polypeptide encoded by the polynucleotide of SEQ ID NO:18 belongs is a family in which the members have divergent functions based on which tissues express said polypeptide or the presence of a particular mutation. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. Although all members may be calcium ion transporters, their effect on cellular function is different. The determination that a polypeptide is a member of T-type calcium family does not give the polypeptide utility in itself. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family.

Applicant arguments that there is no per se rule that partial DNA sequences lack utility and that methods of identifying the full length sequence have utility are not found persuasive. Applicant argues that SEQ ID NO: 18 encodes most of the alpha subunit required for function and that enough information is provided to complete the sequence has been fully considered but not found persuasive. These utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the claimed

polynucleotide. The disclosed protein, whose cDNA has been isolated, is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, a specific and substantial credible utility might be found for the claimed polynucleotide. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The method of identifying the full length sequence of a partial DNA sequence encoding a protein with no disclosed function also has no immediately apparent or "real world" utility as of the filing date because once the complete DNA sequence encoding said protein is isolated further experimentation is required to associate functionality to said protein.

Applicant further argues the use of claimed invention as biological target for screening libraries of compounds as candidate pharmaceuticals. Applicant claims the claimed invention has a clear nexus to specific disease states and "All of the T-type calcium ion channels have the same connection to disease states". Applicants arguments have been fully considered but not found persuasive. As disclosed above the calcium channels have diverse effects. Applicant has not disclosed any specific disease state involved in dysfunction of claimed invention.

Applicant arguments that no *prima facie* case of lack of credible utility has been set forth by the office has been fully considered but not found persuasive because lack of a credible utility is not the basis of instant rejection, rather the basis is lack of specific and substantial utility. The instant application does not disclose the biological role of the polypeptide of SEQ ID NO:19 or its significance. Applicant asserts that the invention has numerous practical, beneficial uses in drug

screening, drug development, and diagnosis of disease, none of which necessarily require detailed knowledge of the complete polynucleotide encoding the claimed calcium channel polypeptide. These utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the claimed polynucleotide. The disclosed polypeptide, whose partial cDNA has been isolated, is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, a specific and substantial credible utility might be found for the claimed polynucleotide. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The DNA of the instant invention and the protein encoded thereby are compounds which share some structural similarity to receptor proteins having calcium channel proteins based on sequence similarity. As disclosed by the specification and Applicants response the family of calcium proteins may have diverse effects, and play roles in the pathogenesis of various diseases, require other subunits for binding of ligands Although the family of proteins having calcium channel protein like domains may share some common structural motifs, various members of the family may have different sites of action and different biological effects. In the absence of knowledge of the ligand for claimed invention, or the biological significance of this protein, there is no immediately evident patentable use. To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for claimed

polynucleotide then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

9. The rejection of Amended claims 28 is maintained under 35 USC § 112, 1st paragraph, in view of the old claim 28, that were rejected in the Office Action mailed 1/17/01, paper number 14, and in view of the rejection that was restated to better address Amended claim 28 in the Office Action mailed 10/23/01, paper number 26.

A summary of Applicants arguments is listed below:

Applicant's has questioned the rejection regarding which statue the citation of *ex Parte Maizel* is used in conjunction with and requested clarification with regard to the enablement of the claimed invention. In response to Applicants question, the claim is rejected under 35 USC § 112, 1st paragraph, as stated on line 6, page 7, paper number 14.

Summary of Applicant's Arguments:

Applicant argues that unlike *Ex Parte Maizel*, the instant limitations of SEQ ID NO: 18 and hybridization under medium stringency conditions provides sufficient structural limitation to enable the full scope of the claimed invention. Applicants arguments have been fully considered but not found persuasive. Applicant has acknowledged that the claim in Maizel was directed to recombinant DNA vector which encode protein having a specified molecular weight and having an amino acid sequence which included what was evidently a portion of a full-length sequence, or biologically functional equivalent thereof which had a specified function. The board found the claim unpatentable under 35 USC § 112, 1st paragraph as overboard. The reason, as stated by Applicant,

was that use of biologically functional equivalent thereof permitted the claim to cover DNA encoding all proteins of any structure whatsoever. The claim was directed to DNA encoding all proteins of any structure whatsoever which had a similar biological activity to the protein for which at least some structural features were described. Applicant states, "That is clearly not the case here" and further states, "The definition of hybridization as "medium" clearly sets metes and bounds on the structure since the nature of medium stringency conditions is well known in the art, and requires a degree of homology defined by these conditions". Applicant further argues that it is not clear what was meant by, "regarding what sequences hybridize specifically to SEQ ID NO:s 18-19 and no other related sequences", and what was referred to by, "not hybridizing to other related sequences".

Response to Applicant's Arguments:

The hybridization conditions of claims 28 are indefinite, as stated in the claim rejection under 35 U.S.C. 112 , second paragraph. The scope of the group of polynucleotides that would meet the limitations of the claim depend upon the precise conditions under which hybridizations were performed, including wash conditions. Hybridization conditions of temperature, salt and time all determine the polynucleotides that remain bound to the DNA of Claim 28 (a). Although medium stringency conditions represent a narrow range of conditions which can be contrasted with high stringency and low stringency, without a specific disclosure of the high stringency and low stringency conditions the scope of medium stringency conditions cannot be determined. To determine the scope of medium stringency hybridization what is required are the specific conditions that form the lower limit of medium stringency hybridization conditions and those conditions that

form the upper limit of , none of which are disclosed. Therefore the term medium stringency hybridization represents the range of conditions X-Y, where X is the lower limit and Y is the upper limit. The question is what conditions of temperature , salt concentration and time represent X and those that represent Y, so as to allow the scope of the claim to be determined. The hybridization conditions recited in the claims do not constitute a meaningful structural limitation. Further the polypeptide encoded by the nucleic acid of SEQ ID NO:18 is incomplete, the functionality of which has not been disclosed, and therefore the claim does not recite a specific functional limitation. Therefore the recitation of medium stringency hybridization without the disclosure of the specific medium stringency hybridization does not impose specific structural limitations on the claim. Without a disclosure of the specific medium stringency hybridization conditions and specific functional language the claims encompass an unduly broad number of compounds. Since the polynucleotide of SEQ ID NO:18 encodes a non-functional polypeptide it can not be assayed for functionality. It follows that the polynucleotides isolated by hybridization, as recited in claim 28, can also not be assigned a function due to the lack of a functional assay. The phrase "regarding what sequences hybridize specially to SEQ ID NO:s 18-19 and no other related sequences", and what was referred to by, "not hybridizing to other related sequences", as used in the context of the rejection in paper number 14, refers to the scope of the claim. The disclosure of a partial polynucleotide sequence (SEQ ID NO:18) encoding a non-functional polypeptide (SEQ ID NO:19), does not support claims which encompass an unduly broad number of compounds (nucleic acids hybridizing to the polynucleotide of SEQ ID NO:18 or polynucleotide encoding the polypeptide of SEQ ID NOs:

19), given the lack of guidance regarding what sequences would hybridize specifically to the polynucleotide encoding the polypeptide of SEQ ID NOs: 19 (i.e. sequences unrelated, structurally and functionally, are encompassed by the claim since the hybridization conditions do not provide a specific structural limitation), and not other, related sequences (the polynucleotides which may hybridize to the polynucleotide of SEQ ID NO:18 encompasses polynucleotides encoding proteins structurally and functionally different to those encoded by the polynucleotide of SEQ ID NO:19, ie. unrelated polynucleotides). Applicant has not disclosed how to use the unrelated polynucleotides which are isolated by hybridization or how to compare their functionality to the polypeptide of SEQ ID NO:19. Therefore like *Ex Parte Maizel*, claim 28, without disclosure of a specific structural limitation (medium stringency hybridization is unduly broad) and a specific disclosed function, the claim encompasses an unduly broad number of compounds.

Written description

10. The rejection of Amended claims 28-33 is maintained under 35 USC § 112, 1st paragraph, in view of the old claim 28-33, that were rejected in the Office Action mailed 1/17/01, paper number 14, and in view of the rejection that was restated to better address the Amended claims 28-33 in the Office Action mailed 10/23/01, paper number 26.

A summary of Applicants arguments is listed below:

Summary applicant's arguments:

Applicant argues that there is no per se rule that in all cases a total reading frame must be disclosed in order to meet the requirements of written description. Applicant further argues that enough information has been provided to obtain full length and to obtain functional equivalents, even if they are not found in nature. Applicant argues that an invention may be complete even with partial structure if other physical, chemical, structural, or functional characteristics are provided, which applicant argues is true in the instant situation. Applicant argues that no precise sequences are required by the claim language and therefore applicant was in possession of the invention as claimed. Applicant also argues that the metes and bounds of the genus are set out by the hybridization conditions and the metes and bounds are framed by a functional activity. Further Applicant states that variations in nucleotide sequences defined by hybridization conditions are standard methods for claiming reasonable genus that includes a single disclosed polynucleotide sequence and do not unfairly extend the metes and bounds of the invention.

Response to applicant's arguments:

The specification discloses a partial DNA sequence (SEQ ID NO:18) encoding the partial α1 subunit of a calcium channel polypeptide (SEQ ID NO:19). The polypeptide is incomplete and lacking functionality. Applicants Response filed 6/11/01 verifies the "amino acid sequence encoded by SEQ ID NO:18 is not complete", and lacks a portion of the amino acid sequence which is required to obtain functionality (See paper number 23, page 4, second paragraph). Therefore, by Applicants own admission, the claimed polynucleotide encoding the polypeptide of SEQ ID NO:19, is

incomplete. Applicant further admits, page 6, the polypeptide is missing "approximately 400 amino acids". Therefore, even though the missing sequence may turn out to be homologous or similar to the C-terminus of other cannel proteins, further experimentation is required to complete the missing sequence.

The claims are drawn to DNA comprising a polynucleotide (SEQ ID NO:18 or complement of a nucleotide sequence that hybridizes under conditions of medium stringency to the polynucleotide of SEQ ID NO:18) encoding a **functional** α1 calcium channel protein. The polynucleotide of SEQ ID NO:18 is incomplete. The function of the functional protein is not disclosed or known. The applicants were not in possession of a functional protein only a partial polypeptide sequence whose functionality has yet to be discovered. Since the polypeptide is incomplete and non-functional there is no disclosure of the critical feature of the invention that is required for functionality. In conclusion Applicants invention is a polynucleotide encoding a partial sequence of a polypeptide who's functionality has yet to be determined but the claims are drawn to a genus of DNA encoding "functional T-type, low voltage activated calcium channel α1 subunit", which clearly does not meet the written description requirement of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing. In response to Applicant arguments, Applicants were in possession of the partial polynucleotide sequence of SEQ ID NO:18 encoding the partial non-functional polypeptide of SEQ ID NO:19. Applicant were clearly not in possession of the functional protein encoded by the total reading frame of the complete protein. An

adequate written description of a DNA, such as the cDNA of instant application, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606. (page 1404). Applicant provide a partial sequence for a non functional protein and claim the genus of polynucleotides encoding functional full length proteins. The structure, formula, chemical name, or physical properties a functional full length protein encompassed by the claims has not been disclosed and therefore an adequate written description of the genus of claimed DNA has not been provided. Applicants argument that the metes and bounds of the genus are set out by the hybridization conditions and the metes and bounds are framed by a functional activity have been fully considered but not found persuasive. As stated in the rejection under 112 first and second paragraphs, see above, the medium stringent hybridization do not provide a meaningful structural limitation to claim a reasonable genus of compounds. The variations in nucleotide sequences defined by hybridization conditions can be used for claiming reasonable genus that includes a single disclosed polynucleotide sequence and do not unfairly extend the metes and bounds of the invention if the hybridization conditions are clearly defined so as to allow the metes and bounds of the claim to be determined, coupled with a functional limitation, such is not the case in instant invention. Further, since the claims are drawn to a polynucleotide encoding a functional

calcium channel protein the claims were also rejected for encompassing the gene encoding the polypeptide of SEQ ID NO:19. The gene encoding the polypeptide of SEQ ID NO:19 is a DNA molecule comprising an expression system for the production of a functional calcium ion channel α1 subunit. Only the polynucleotide consisting of the polynucleotide of SEQ ID NO:18 and the polynucleotide consisting of the polynucleotide that encode the polypeptide of SEQ ID NO:19 meet the written description requirement. Polynucleotides comprising the polynucleotide of SEQ ID NO:18 or polynucleotides comprising the polynucleotide encoding the polypeptide of SEQ ID NO:19 do not meet the written description requirement for reason given above and reasons presented in paper number 26.

Claim Rejections - 35 USC § 101 (New Rejection)

11. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 28-30 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 28-30 recite a DNA molecule which comprises an expression system but do not recite that they are isolated or purified. The claims as currently recited encompass these naturally-occurring compounds (chromosomes). Therefore, the compounds as claimed are a product that occurs in nature and does not show the hand of man, and as such is non-statutory subject matter. It

is suggested that the claims be amended to recite "an isolated and purified" to overcome this rejection.

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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